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(54) Title: GLYCOGEN SYNTHASE KINASE-3 INHIBITORS

(57) Abstract: Novel conjugates that are capable of inhibiting GSK-3 activity, a process of producing same, pharmaceutical compositions including same and methods of using same in the treatment of GSK-3 mediated conditions are disclosed. Methods of treating affective disorders using GSK-3 inhibitors are further disclosed.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL 03/01057

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/47 C07K7/06 C12Q1/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE, EMBASE, WPI Data, CHEM ABS Data, BIOSIS, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | WO 01/49709 A (ELDAR FINKLEMAN HAGIT ;UNIV RAMOT (IL); MCINNIS PATRICIA A (US)) 12 July 2001 (2001-07-12) the whole document | 1-166 |
| X | WO 02/24941 A (UNIV DUNDEE ;BIONDI RICARDO (GB); FRAME SHEELAGH (GB)) 28 March 2002 (2002-03-28) the whole document | 1-166 |
| X | OELRICHS P B ET AL: "UNIQUE TOXIC PEPTIDES ISOLATED FROM SAWFLY LARVAE IN THREE CONTINENTS" TOXICON, ELMSFORD, NY, US, vol. 37, no. 3, 1999, pages 537-544, XP000994829 ISSN: 0041-0101 figure 3 | 1-5, 10-13 |
| | --- -/- | |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *&* document member of the same patent family

Date of the actual completion of the international search

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Date of mailing of the international search report

04/06/2004

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/IL 03/01057

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | <p>ELDAR-FINKELMAN H ET AL: "The insulin mimetic action of glycogen synthase kinase-3 inhibitors" DIABETOLOGIA, vol. 45, no. Supplement 2, August 2002 (2002-08), page A 70 XP009031166 38th Annual Meeting of the European Association for the Study of Diabetes (EASD);Budapest, Hungary; September 01-05, 2002 ISSN: 0012-186X abstract</p> | 1-142 |
| T | <p>PLOTKIN BATYA ET AL: "Insulin mimetic action of synthetic phosphorylated peptide inhibitors of glycogen synthase kinase-3." JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, vol. 305, no. 3, June 2003 (2003-06), pages 974-980, XP009031218 ISSN: 0022-3565 (ISSN print) the whole document</p> | 1-166 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL 03/01057

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ IL 03 /01057

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although independent claims 88, 118 and 142 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds.

Continuation of Box I.1

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IL 03/01057

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
|---|---|---------------------|---|--|
| WO 0149709 | A | 12-07-2001 | AU 2625201 A WO 0149709 A1 US 2002147146 A1 | 16-07-2001 12-07-2001 10-10-2002 |
| WO 0224941 | A | 28-03-2002 | AU 8791401 A WO 0224941 A2 | 02-04-2002 28-03-2002 |